Generic competition in pharmaceutical industry - How long does it take for generic drugs to enter the market after having applied for Market Authorization in Norway?

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ABSTRACT

Background: Historically in Norway, pharmaceutical prices have been particularly high for originator drugs, which are produced by originator companies that have a monopoly through the patent system. However, once the patent expires, generic drugs are able to enter the market and cause a considerable decline in price. The Norwegian Medicine Agency (NoMA) is responsible for issuing market authorization (MA) and inclusion in the reimbursement scheme, for any new drugs in Norway. NoMA must evaluate the cost-effectiveness analysis of the originator drug provided by the pharmaceutical company. In order to predict cost-effectiveness, it is important to estimate how long the originator drug will stay in the market before generic competition is established.

Objectives: Investigate how long it takes for a generic drug to enter the market after applying for MA, and what are the potential reasons for the time span used.

Methodology: A combination of qualitative and quantitative study design. Empirically based and a single-case study. There were in-depth interviews conducted with executive officers at NoMA and representatives from generic and originator firms. The quantitative data was collected from the NoMA´s databases, namely Athene and P360. The data was divided into four phases and a statistical description of each phase was created. Furthermore each phase was divided into two periods 2005-08 and 2009-12 for the purpose of running a Man Whitney U test in order to reveal the time differences between the two periods.

Results: For quantitative analysis the following was found: (1) For a generic medicine to obtain MA it takes 357 days according to median. (2) A generic drug used 131 days (median) to enter the market after MA approval. (3) Additionally in the second period 2009-12 it took longer time to obtain MA and enter the market compared to the first period of 2005-08. For qualitative analysis the following was discovered: (1) Various obstacles which affect the MA process. (2) Patent obstacles and complications which affect the overall time span. (3) Norway is a relatively small market and therefore less attractive for some generic companies. (4) Production issues and challenges faced by generic firms. (5) In some cases, the substitution list and reimbursement scheme processes can cause delays to the overall time span. (6) Once the original drug patent expires, the original firms can choose to enter the stepped price system and create competition for generic firms, which causes a delay in entering the market.

Disclaimer: The findings, interpretations and conclusions expressed in this paper are entirely those of the author and not represent the views of Norwegian Medicines Agency

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List of Abbreviations

ATC	Anatomic Therapeutic Chemical
EEA	European Economic Area
EU	European Union
MA	Market Authorization
MOH	Ministry of Health and Care Services
NIS	Norwegian Insurance Scheme
NoMA	Norwegian Medicines Authority
NSD	Norwegian Social Science Data Services
RHA	Regional Helath Authorities
WHO	World Helath Organization

1. Introduction

1.1 Background

Historically pharmaceutical prices have been especially high for the originator drugs, produced by originator companies that have a monopoly through the patent system. However, after the patent expires, generic production firms can develop generic drugs with the same medical effect and substance as the originator drugs. When this occurs, the generic drugs are considerably cheaper than the original drugs, therefore providing an alternative choice with a big decline in price, for the consumer.

Furthermore there are other mechanisms that affect the price such as the comparative drug mechanism, were another drug producer develops a drug with a similar effect as the originator but using a different chemical substance (Informant at NoMA). Moreover, there is a parallel import mechanism of the original drug i.e. the same drug is produced in another country in a cheaper manner and imported to Norway (Ot.prp. nr. 29 (1998-99)).

The Norwegian Medicine Agency (NoMA) is responsible for issuing market authorization (MA) and inclusion in reimbursement scheme for any new drugs in Norway. To perform this NoMA must evaluate the cost-effectiveness analysis of the drug provided by the pharmaceutical company. This analysis considers a historical period of several years to evaluate the effects of the drug for the patients. Additionally, the analysis takes into account the asking price of the producer for the drug, in order to evaluate its cost-effectiveness. In order to predict cost- effectiveness, it is important to estimate how long the drug will stay in the market before generic competition is established.

It would be of importance for NoMA to estimate the time span from the date the generic firms apply for MA until the date the generic drug enters the market. This would assist NoMA to predict a better price path of a comparativ drug who applies for reimbursement. This is the

purpose of the thesis, which to my knowledge it is being conducted for the first time in Norway.

1.2. Objectives and hypothesis

NoMA was interested to find out how long it takes for a generic drug to enter the market after it applies for MA. With the result of this paper NoMA wish to make more adequate decisions in evaluating the pharmacoeconomic evaluations of a new drug, especially for a comparative drug when it applies for reimbursement.

The focus of this thesis will be to study the process of a generic drug entering the market in Norway. The study will also consider and estimate how long it takes for pharmaceutical companies to obtain Market Authorization, as well as how long it takes for a pharmaceutical company to launch the generic and for the stepped price system to be established.

The research question of this thesis is:

ñ*How long does it take for generic pharmaceutical companies to obtain Market Authorization and enter the stepped price system?****ò***

The aim of the study is to analyse and describe the processes in question and evaluate if these processes can be formalized and utilized to predict the price path (prisbaner) when evaluating health economic analyses. The following sub-questions have arisen to answer the research question:

1) How long does it take for a generic to enter the market after the original is established?
2) How long does it takes for generic to get approved Market Authorization, how does this process proceed and why?
3) How long does a generic use to enter the market after approved Market Authorization and why?

4) Is there any difference in time span of these processes between the period of the stepped price system establishment in 2005-08 and the period after it was well-established in 2009-12?

The sub-question number four is used as a hypothesis in the quantitative methodology of this thesis, formulated as:

Null hypothesis: there is no difference in time spans between the periods 2005-08 and 2009-12.

Alternative hypothesis: there is a difference in time spans between the periods 2005-08 and 2009-12.

The motivation and policy of this thesis is based on Martin Holyeôs article about the ñFuture drug prices and cost-effectivenessò where he describes that drug prices are more cost effective than NICE (National Institute for Health and Care Excellence in UK) stated. Generic drugs are one of the reasons why drug prices fall (Hoyle, 2008).

1.3. Methodology

In this paper a combination of qualitative and quantitative study design will be employed. The qualitative part of the study design will be descriptive. Both study designs will be based on a retrospective reference period. In the quantitative part of the thesis, the data is obtained for all the substances that entered the stepped price system from May 2005 until December 2012 using the Norwegian Medicines Agency (NoMA) database, namely Athene and P360. For each phase of the overall process, an estimation of the descriptive statistic was generated and each phase was divided into two periods 2005-2008 and 2009-2012. The Mann Whitney U test was run to examine if there is a difference in time span between the two periods.

The four phases of the overall process are:

- The date the originator firm obtained market authorization until the date the originator drug entered the market.
- The date the generic firm applied for market authorization until the date the generic firm obtained approval.

- The date the generic firm obtained market authorization until the date the generic drug entered the market.
- The date the original drug entered the market until the date the generic competition started.

Furthermore, in qualitative part of the thesis in-depth interviews were conducted with executive officers at NoMA who work with MA, substitution lists, the stepped price system and with representatives from generic and originator production firms. The purpose of the interviews conducted was to find out more about the system and the reasons behind each time span that was used for the generic products to enter the market.

1.4 Structure of the thesis

Chapter one is introduction of the thesis. The next chapter, Institutional framework, will be a description of the Norwegian pharmaceutical market and the mechanisms needed for a medicine to enter the market. Chapter 3 illustrates the institutional framework for generic medicines in Norway. Chapter 4 consist of motivation and policy to write this thesis. The methodology used to develop this paper is described in chapter 5. Results of the thesis are presented in chapter 6, both quantitative and qualitative. The conclusion is presented in chapter 7.

2. Institutional framework

2.1. The Supply side

The supply side consists of pharmaceutical producers, wholesalers and retail pharmacies.

2.1.1 Pharmaceutical industry

The pharmaceutical sector is extensively regulated and driven by high research and development (R&D). There are two types of companies on the supply side, originator companies and companies that manufacture generic products. The originator companies are responsible for R&D and managing the regulatory process of new innovative products required by the authorities. The responsibilities include clinical trials, MA, manufacturing, marketing and supply. The generic companies enter the market after the patent of the original product expires, as well as the data exclusivity period expires for the original product. The generic medical products are equivalent to the original products, but have much lower prices (European Commission, 2009).

2.1.2. The patent of pharmaceuticals

Pharmaceutical companies that invent new substances can apply for patent protection, which covers them for 20 years. However in order to develop and release a pharmaceutical product in the market, it may take between 8 to 12 years for a pharmaceutical company to carry out R&D. Therefore out of the 20 years of patent protection, the company is left with only 8 to 12 years of monopoly in the market. Once the patent expires, generic competition can enter the market (Brekke, Holmås and Straume, 2007).

The pharmaceutical industry generally refers to two types of patents. ñPrimary Patentsò are types where the patent is concerned with the active substance. ñSecondary Patentsò are types where the patent is concerned with aspects such as the production process, different dosage forms or for particular pharmaceutical formulation (European Commission, 2009).

The European patent law system is adapted to a great extent in Norway but not fully applicable (Brekke, Holmås and Straume, 2007).

2.1.3 Producers in Norway

In Norway pharmaceutical industry is represented by major international companies, from which a few have established their own manufacturing units in the country. The 4 main suppliers in 2011 were:

- Pfizer with 9.8% of the market share
- MSD 7.4% of the market share
- Novatis Norge AS with 7.0 % of the market share
- GlaxoSmithKline AS with 5.7% of the market share

The 3 main production facilities in Norway are General Electric, Nycomed Pharma and Fresenius Kabi (PHIS Pharma Profile Norway, 2011). The Norwegian Association of Pharmaceutical Manufacturers- LMI represents most of the pharmaceutical industry, which are research-oriented companies in Norway (LMI, 2013).

2.1.4. The wholesalers and retail pharmacies

After the introduction of the current pharmaceutical act in 2001 the Norwegian pharmaceutical market developed a vertically integrated market. There are now 3 wholesalers with their own pharmacy chain in Norway. The law prohibits direct distribution of pharmaceuticals from manufacturers to the end user in general. The distribution chain to end-users goes therefore through wholesalers and the pharmacies they own (PHIS Pharma Profile Norway, 2011).

The below table describes the ownership structure of the wholesalers in Norway in 2011:

Table 2.1. Ownership structure

Pharmaceutical chain	Wholesaler	Owner	Market share
Boots apotek	Alliance Healthcare Norge AS	Alliance Boots Limited (UK)	23.7%
Vitusapotek	NMD Grossisthandel AS	Celesio AG (German)	47.6%
Apotek 1	Apokjeden DistribusjonAS	Tamro OY (Finish)/ Phoenix (German)	28.9%

Source by Apotekforeningen and PHIS Pharma Profile Norway 2011

2.2. The government

The aim of government health policies regarding pharmaceuticals is to promote correct use of medical products. The governmental overall objectives are:

- Low pharmaceutical prices
- Reliable access to efficient medical products independent of patients' ability to pay
- Promotion of correct use of medicines both medically and economically

The Norwegian government reimburses the use of pharmaceuticals through the National Insurance Scheme (NIS). Generic competition contributes to lower the prices of off-patent pharmaceuticals. As a result less money is spent reimbursing these medicines and there are more opportunities to invest in new drugs or treatments.

The Ministry of Health and Care Services (MOH) is responsible for managing the pharmaceutical politics through law regulation in the field and reimbursement. Many of the tasks are delegated to the underlying professional body called the Norwegian Medicine Agency, NoMA (St.meld.nr 18 (2004-2005)).

There are two main national laws that regulate the pharmaceutical market including pricing and reimbursement, namely the Norwegian Pharmacies Act and the Norwegian Act on Medical Products (PHIS Pharma Profile Norway, 2011).

2.3. The Norwegian Medicines Agency (NoMA)

The Norwegian Medicines Agency is the underlying body of Ministry of Health and Care Services covering pharmaceuticals and represents Norway in European Union (EU).

NoMA is responsible for approving MA for pharmaceutical products, ensuring that any medicine used in Norway is of high quality, is safe to use and has the adequate effect. Additionally, NoMA is responsible for setting the maximum pharmacy purchase prices and maximum reimbursement prices for affected medicines, both original and generic. Reimbursement decisions are made by NoMA only when expected sale for the medicine is less than 5 mill NOK per year in the next coming 5 years, otherwise the Storting, Norwegian parliament after proposal from Ministry of Health makes a decision on reimbursement. The pharmaceutical companies need to follow the Norwegian guidelines for pharmacoeconomic evaluation when applying for reimbursement (NoMAa, 2013).

2.4. Market authorization (MA)

Producers that are interested to sell their pharmaceutical products in the Norwegian market must apply for MA at NoMA. The requirement for the application form, its design and content must follow the EU requirements, as Norway is a member of the European Economic Area (EEA). For NoMA to be able to release the MA, the producer must document pharmaceutical quality, security and medical effect of the medicament. Adding to the submitting application the following documentation on chemical, pharmaceutical, biological, preclinical and clinical documentation. The MA is released only if the benefit of the medicine is greater than the risk posed to the patient (MOHa, 2013).

There are several alternative procedures required in order to submit the application for MA. The pharmaceutical firm can apply for one of the procedures depending on magnitude of the

marked the firm is willing to enter. The procedures are: national procedure, mutual recognition procedure, central procedure and decentralized procedure. Below is a summary of each:

1. The National procedure: the application is submitted to one country and the MA of the medical product is limited only in one member state of EEA. This is the initial phase of the mutual recognition. For the national procedure there is a requirement of 210 days to release MA for a product (European commission, 2005).
2. The Mutual Recognition procedure: After granting of the national MA by an EEA reference member state, the producer can ask the concerned member states to issue the MA using the national procedure of the reference member state. For mutual recognition it is a requirement of 90 days to recognise the reference MA in the concerned member states (European commission, 2005).
3. The Centralized procedure: the application should be submitted to the European Medicine Agency (EMA) for products that fall into the mandatory and optional scope of the centralized procedure. Two chosen member states of the EEA examine the application together with the expert committee of the EMA. The EMA then drafts a decision on MA based upon the receipt of opinion from the chosen states and following scientific evaluations. Norway and Iceland are an exception as they are not part of EU and therefore must approve the MA within 30 days after a decision is drafted by EMA (European commission, 2005).
4. The Decentralized procedure: the application is directed to several member states but only one state is in charge of assessing the application. MA will be approved only for the states applied for. This procedure helps to increase the cooperation and effectiveness between the member states (European commission, 2005).

For this phase the NoMA and the EMA are responsible for the time span used. Once the firm hands in the application form for MA, NoMA and EMA have 210 days to respond. The firm has to send in all the required documents for the application. If any documentation is lacking, the firm is contacted to bring in the missing documentation. In these cases the NoMA starts a so-called clock-stop period, which means the case will freeze until the firm responds and NoMA starts the clock again. The clock measures the time spent processing the application. In reality, the process of getting MA will exceed the 210 days, if we measure the total days

used between applying and receiving MA. (European commission, 2005; informant at NoMA, 2012)

Application procedures for MA are the same for generic drugs as for the original drugs, but in addition for generic drugs itôs a requirement to document the bio similar effect of the original drug (NoMAb, 2013).

2.5. Pricing

NoMa determines the maximal pharmacy-purchasing price for all prescription-only medicines in the Norwegian market. Since 2002 the price has been decided by the external reference price system of 9 countries including: Austria, Belgium, Denmark, Finland, Germany, Ireland, the Netherlands, Sweden and the United Kingdom. The price for the Norwegian market will be extracted from the average of the three lowest pharmacy-purchasing prices of these countries. The price comparison is made per unit (tablet/dosage), since pack sizes in different countries are not directly comparable. Normally price changes are made once a year and may result in lower or higher prices. The purchasing price from producers to wholesalers is not regulated by the government, and the wholesalers negotiate freely the mark-up of the product with the production firms. The pharmacy retail price is also set at NoMA by adding the maximum mark-up to 7% for medicines with pharmacy-purchasing prices below 200 NOK and up to 4% for medicines with pharmacy-purchasing prices above 200 NOK. The pharmacies can freely sell the medicine at a lower price than the one NoMA sets. Prices of generic products cannot exceed the maximum market price of the original products (PHIS Pharma Profile Norway, 2011).

Once the medicine is granted MA, it can apply for a price at NoMA. The maximum processing time for price application is 90 days, however the average processing time in 2010 was 32 days (PHIS Pharma Profile Norway, 2011).

2.6. Pharmaceutical Reimbursement

Reimbursement of pharmaceuticals in Norway is one of the implements to reach the main governmental goals for pharmaceuticals. The government funds about 70% of the total pharmaceutical costs in Norway. Funding responsibilities are threefold between the Regional Health Authorities (RHA), the Municipalities and the National Insurance Scheme, NIS (Norwegian Directorate of Health a, 2012).

The RHA are responsible for funding the pharmaceuticals used during the hospital stay. The hospitals budget covers hospital medicines. Municipalities cover the medicines for the people living in Long Term Care institutions (Norwegian Directorate of Health a, 2012).

The NIS covers the pharmaceutical costs for out-patient care only for prescription of pharmaceuticals. A patient co-payment ceiling scheme was introduced in 1980s for all Norwegian citizens covered by NIS (Norwegian Directorate of Health, 2012). The scheme covers all patient costs for health care services as: doctor visit, psychologist visits, hospital stay, radiology department and pharmaceuticals in reimbursement scheme once the cost ceiling has surpassed. The cost ceiling is 2040 NOK per patient for the year 2013 (Helfo, 2013). Norwegian patients pay out of pocket 38% of the pharmaceutical price or max 520 NOK per prescription, until they reach the cost ceiling. Then the NIS will fund all the pharmaceuticals in the reimbursement scheme that surpass the cost ceiling. The purpose of the scheme is to get a small contribution from patients in order to avoid unnecessary use of health care resources (Norwegian Directorate of Health a, 2012).

For all new medicines that enter the Reimbursement Scheme, NoMA makes an assessment of cost effective analysis made by the pharmaceutical producer. NoMA is allowed to grant reimbursement for a medicine if the cost of reimbursement does not exceed the Norwegian so called ñbagatellgrensenò. Bagatellgrensen is a ceiling of 5 million NOK costs in reimbursement per year in the 5 coming years for the particular medicine. Medicines that require funding above this ceiling are sent to the Ministry of Health and Care Services in order to make the assessment of cost effectiveness and the final decision of funding the

medicine in comparison with other needs in all sectors of the country (St.meld.nr.18 (2004-2005)).

The criteria for granting reimbursement for new medicines is defined by the Norwegian Pharmacies Act, paragraph 9, listed below:

1. The medicine should be used for treatment of a serious disease or risk factors that most likely will cause or worsen the disease.
2. The disease in question or its risk factor will necessitate the need for repeated treatment over a long period.
3. The medicine is scientifically well documented and has a clinically relevant effect in a defined patient population.
4. The cost of using the new medicine is reasonable compared to the treatment value
5. The cost associated with alternative treatment (St.meld.nr.18 (2004-2005)).

Generic medicines will enter the reimbursement scheme once the MA is approved. There is no need for an economic assessment for generic medicines as the price is much lower than the original medicine.

3. Generic medicines and the institutional framework

The European medicine agency defines a generic medicine as: a medicine that is developed to be the same as a so-called reference medicine, which has already been authorized. Further, a generic medicine must contain the same active substance and doses to treat the same diseases as the reference medicine. However, the difference from the reference medicine can be the name, inactive ingredients, appearance and packaging of the generic medicine. Generic medicines have the same manufacturing quality standards as all other medicines. They can first be developed for the market after the period of exclusivity on the reference medicine has expired (European Medicine Agency, 2013).

In Norway, the Pharmacies Act was introduced in 2001 which regulates automatic substitution between original and generic drugs when dispensing pharmaceuticals in pharmacies. Usage of generic products is of great economic interest for payers, in this case the Norwegian health insurance scheme. Approximately 2 billions NOK are saved per year using generic medicines in Norway, which 75% of these are saved by NIS and 25% by the patient (NoMAc).

3.1. The stepped price system

The stepped price system model (Trinnprismodellen) is a scheme that ensures price fall in pharmaceuticals stepwise by predefined rates. The model was introduced in January 2005 to reduce the costs of National Insurance Scheme and it applies only after generic competition is introduced. The step price model applies for all active substances with generic competition, with the exception of some substances where it is not convenient to include in the model. Initially when the scheme began, 21 substances were included in the system. The system has now expanded with more substances since then (MOH b, 2013).

The stepped price is determined when the first generic product enters the market. The stepped price is a percentage of the maximum price of the original drug at the time. The first price fall occurs as soon as the generic enters the market and is 30%. The second price fall occurs after

6 months and depends on the size of the turnover of the active substance before generic competition occurred. In addition there might be a third price fall 12 months after the second price fall if the appropriate active ingredient is sold for more than 15 or 30 million NOK (NoMAc).

The diagram below describes how the stepped price system is applied:

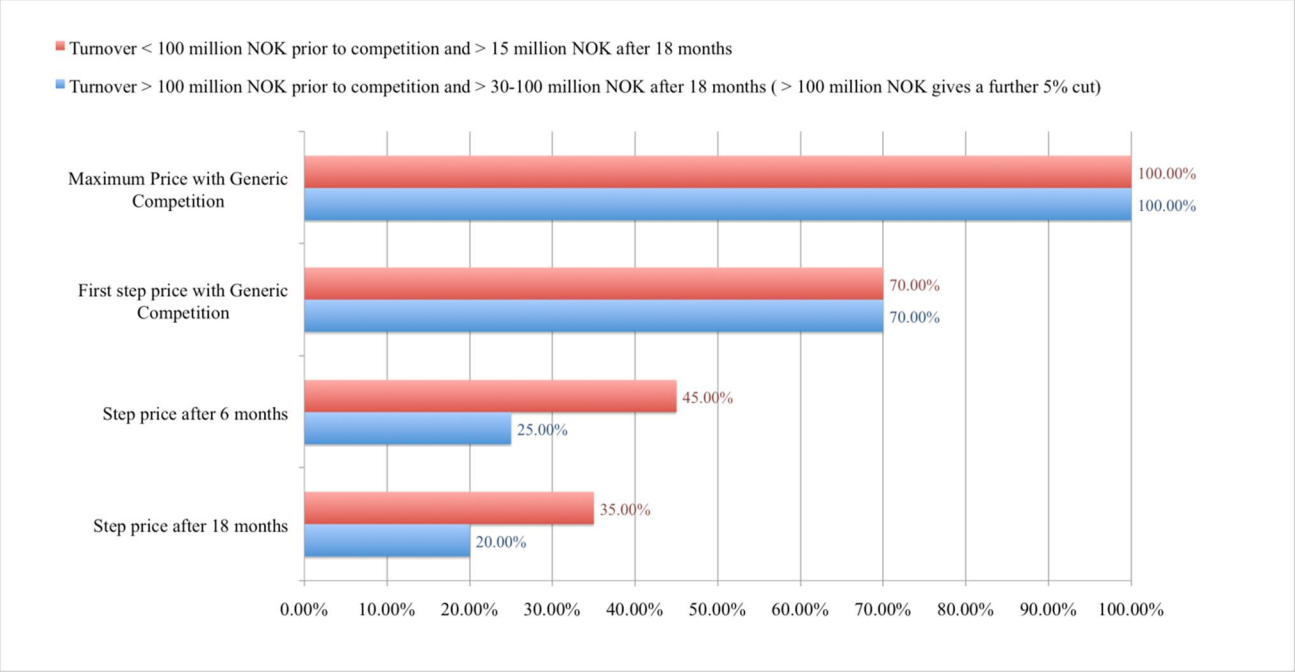

Figure 3.1. Stepped price system in Norway. Source by NoMA

In order for generic pharmaceuticals to enter the market, the producers of generics have to come to a selling agreement with the wholesalers. When an original product has almost reached the end of its patent period, its generic products can start the process of entering the market. Firstly, the firms with a generic product must have MA and a set price, as well as be eligible for reimbursement. Secondly, the firms must send their offer to wholesalers where they present their price and conditions, and the negotiations start. The best offer is chosen, and the wholesalers make an agreement with the generic firm usually for a one-year period. It is very important for the generic firms to get the agreement first. This will give them an advantage in the market, as the consumer or patient will be familiar with their product. In the

future when more generics will enter the market it will be easy for consumers to choose the product they are familiar with (Subtracted from the conducted interviews).

Once the generic product enters the market, the pharmacies are obliged to sell the cheapest product at stepped price, because that is the price that is being reimbursed by the government (St. meld. nr. 18 (2004)). If the patient would like to use the original product which is usually the expensive one, then he/she will have to pay the difference in the price i.e. if a generic product costs 70 NOK, and the original 100 NOK, the pharmacies have to offer the patient the cheapest one, regardless of which product the doctor prescribed. The patient then has a choice to accept a 70 NOK product or go for the original product, which costs 100 NOK. The patient would then have to pay 30 NOK from out of pocket.

3.1.1. Inclusion of pharmaceuticals in stepped price system

The Pharmaceutical Act, paragraph 12-15 determines the routines of inclusion of new substances in the stepped price system (NoMAd, 2013). All substances in the stepped price system have the following in common:

1. The drug is in the substitution list.
2. The original drug has stable generic competition from at least one drug in the Norwegian market.

Before NoMA notifies the wholesalers of the inclusion in the stepped price system for a substance, a closer examination of the case of the generic is performed by:

- Checking the Farmastat statistics if there have been registered generic sales.
- Generic companies confirm in written form they are ready to deliver the generic product when contacted. - There have been situations in the past where generic companies were ready to deliver but the wholesalers chose to continue the agreement with the original company. This meant they continued to sell the original product at the stepped price level from the moment the generic companies were ready to deliver. Therefore the stepped price system model starts with the original drug excluding generic competition. According to the Pharmaceutical Act, if a generic is on the

substitution list and is ready to be delivered, it is sufficient for the stepped price system to be implemented (NoMAd, 2013).

Furthermore, in some cases the applicable stepped price for a generic is too low and as a result it is not profitable to sell in Norway. In these cases NoMA has the authority to set a subjective price for the generic. This authority is based on the Pharmaceutical Act (NoMAd, 2013).

Once NoMA has established that a generic is selling in the market or the generic company has informed NoMA that it is ready to sell, the notification process begins. The process is summarised below:

1. Pharmaceutical suppliers (both original and generic) get a notification via e-mail. They get 14 days to respond and comment on the notification.
2. The reference group for stepped price, wholesalers and MOH are included as copy receivers of the e-mail. They can also respond and comment on the email within 14 days.
3. Comments are received by e-mail or letter.
4. NoMA considers the responses and undertakes further decisions that are sent to suppliers by e-mail, including the stepped price reference group, wholesalers and MOH.
5. The prices are sent to Farmalogg. The new stepped price enters the market on the 1st or 15th of the next month (NoMAd, 2013).

3.2. The substitution list (Byttelisten)

A medicine enters the substitution list scheme only if it is bioequivalent, medically equal and suitable for safe substitution in the pharmacies. NoMA ensures this in Norway.

Two medicines are bioequivalent when their bioavailability is equal to the effect and security as a whole. This is determined by the studies that are carried out based on the common European guidelines. These studies confirm whether the body equally absorbs the active substance from both the original and the generic medicines (NoMAe, 2013).

Two medicines are substituted when they:

- Contain the same active substance in dosage and strength. Only medicines with the same strength are automatically interchangeable in pharmacies.
- Have the same medical form (capsules and tablet with fast substantial release are considered equal).
- Have the same package size (+/- 20%). The pharmacy has to deliver enough medicines to a patient to ensure the treatment plan. In case of delivering a larger size than subscribed from the doctor, the pharmacies have to inform the patient not to use the leftovers of the medicines (NoMAe, 2013).

An interdisciplinary group (Byttegruppen) using adequate guidelines decides if a medicine is equal and interchangeable, then passes their recommendations to managers at NoMA. The process is elaborated in several group meetings. This happens after a medicine obtains market authorization and price. The interdisciplinary group consists of pharmaceutical, medical, regulatory and jurisdiction competence. Certain types of pharmaceutical products are consumed in a unique way and as such cannot be automatically substituted with other products. These cases are sent to a hearing to determine whether the product is suitable to enter the substitution list or not (NoMAe, 2013).

4.Motivation and policy relevance of the thesis

Martin Hoyle (2008) argues in the following article ñFuture drug prices and cost-effectiveness analysesò that most of the drugs were more cost-effective than the National Institute for Health and Clinical Excellence (NICE) stated. Hoyle calculated the real-price change of 373 drugs in the UK between 1980-2006. Based on calculations the historic mean of the real-price change, across the drug products launched after 1984 with more than 500 prescriptions per year, his findings suggested that a future real-price of a drug should have a decreasing rate of 4% per annum. However, when a drug patent is expected to expire in the near future, a generic drug will enter the market and the cost-effectiveness analyses should include the best-estimated price decline of the generic (Hoyle, 2008).

The Norwegian Ministry of Finance in its public report about socio-economic (samfunnsøkonomiske) analysis discusses the real-price adjustment of a good or service (realprisjustering) in chapter 4 (NOU 2012:16, 2012). A real-price adjustment is an adjustment of a calculated price that might grow in a different direction from the consumption price index. In order to compile the future benefit and cost of a project, one should make assumptions about how estimated prices will evolve differently during the period of the analysis. For the sake of simplicity the prices are usually kept constant. If the prices of a good or service rise relatively to the other goods or services during the analysis period, then the project appears less beneficial then it really is (NOU 2012:16, 2012).

4.1 Why include the time spans in this thesis?

The importance of the time span when evaluating cost effectiveness is stated by guidelines when NoMA reimburses the medicines.

The Norwegian Health Directorate prepared a guide of health economic evaluation in which the time horizon of a health care programme is discussed.

When calculating cost effectiveness in cases where there is a comparison between two or more health care programme alternatives, the time horizon of the programme outcome can

affect the cost-effectiveness. Therefore the time horizon should be long enough to capture the important differences between the alternatives, in cost and health effects. A programme can be of short duration, one or two years, but still have lifelong perspective consequences. A lifelong perspective is always suggested when a programme affects the life expectancies and the quality of life of the remaining life years (Norwegian Directorate of Health b, 2012).

In order to make a better assessment in price paths for pharmaceuticals, it is important to be aware of the factors that affect the price path. Therefore an estimation of time span used for generics to enter the market from the time they apply for MA is of important value when issuing reimbursement for pharmaceuticals.

This paper is based on Hoyleôs findings and the requirement from the Ministry of Finance about the real-price for services in Norway.

5. Methodology

5.1. Study design

The focus of this thesis will be to study the process of a generic pharmaceutical entering the market in Norway. The study will also consider and estimate how long it takes for pharmaceutical companies to obtain Market Authorisation and also how long it takes for the stepped price system to be established.

To obtain the required information for the study, relevant data was collected from the NoMAsô database on each substance in the stepped price system in Norway from 2005 to 2012 and the range and median was determined for each time span. In addition, further information was collected in an attempt to find answers to the question of why generics used a particular time span to enter the market.

To ascertain a more accurate and complete investigation a combination of quantitative and qualitative research approach was used and the single case study design was chosen to gain insight and a better understanding of the process. The reference period of the study is retrospective since the investigation is based on the existing data from the period May 2005 to December 2012 (Kumar, 2001).

A research approach is classified as quantitative if the purpose of the study is to quantify the variation in a situation or phenomenon, and if the analysis is adapted in order to match the magnitude of the variation (Kumar, 2001). This research approach was employed and presented through the systematic data collection at NoMA for this thesis.

Furthermore, a combination of quantitative and qualitative research approach was used. Quantitative research approach is used, according to R Kumar when ñ*you want to quantify the variation in a phenomenon, situation, problem or issue; if information is gathered using*

*predominantly quantitative variables*ò (Kumar, 2001:13). Quantitative data is used to find the time span of four phases in-between, from when the original drug entered the market until the generic competition was established and statistical tests are performed to find and present the different findings of the four phases. A research approach is classified as qualitative if the aim of the study is to describe a situation or phenomenon where the analysis is done to establish the variation without quantifying it (Kumar, 2001). The qualitative research approach was appropriate to use in this thesis in order to describe the expert views of the system through a single case study.

Based on R Kumarôs book, the objectives set define the type of research for this thesis as a combination of both descriptive and exploratory study. This thesis is a descriptive study, as it is an attempt to systematically describe an existing situation or phenomenon and provide insights about potential issues (Kumar, 2001). The study has an exploratory approach as defined by R Kumar ñ*a study where objectives are to explore in an area where little is known*ò (Kumar, 2001:10).

A single case study is used in both qualitative and quantitative studies for an exploration of the in-depth and general aspects of what the researcher wants to find out. Moreover, a single case study design is useful when little is known and the researcher wants to gain a holistic understanding of the situation or phenomenon (Kumar, 2001). This study design is appropriate for this thesis, since I am the first to gather the data systematically from NoMA and in order to provide insightful findings in the current situation of the time span used by generics before entering the market.

In order to reach the set objectives, gathering of more information on the process was necessary. Oral history method data collection seemed suitable. I decided to obtain this data by gathering information from professionals working with generic drugs and addressing a variety of questions about their experiences with generic competition and the stepped price system. Oral History method of data collection enables the researcher to study experiences and gather the historical knowledge of an event, as viewed by individuals. This process involves the identification of the type of experience or historical event the researcher wants to

find out and the identification of individuals who are able to give her/him best information needed (Kumar, 2001).

In order to collect the data through oral histories, in-depth and semi-structured interviews were conducted with professionals in the field. The decision of using semi-structured interviews was made to give the informant the freedom to speak within the topic of the thesis.

5.2 Hypothesis difficulties

In the beginning of the process of writing this thesis several hypothesis ideas were tried in order to capture all the questions attempted to answer in this thesis. Furthermore, it was attempted to generalize the results of the elapsed time span used to enter the market for all generics. However the qualitative data was limited and skewed, and covered only one part of the thesis. Later on, it proved to be difficult to choose a hypothesis that covered all the issues, as the pharmaceutical system is quite complex and many aspects affect it.

The thesis was designed to describe the data and dividing them into phases, thereafter each phase into two time periods from 2005-08 and 2009-12, in order to determine if there was any difference in the process between the two periods. The process here refers to the time used for generics to receive MA and the time used for generics to enter the market after receiving MA. Another important part of the thesis was the information conceived by the interviews, which fulfilled the quantitative results.

5.3. Quantitative data selection

The data selection included only out-patient drugs with generic competition which are part of the stepped price system. The data was collected manually from the database Athene and P360 at NoMA. It includes all the substances based on the Anatomic Therapeutic Chemical (ATC) codes in the market, which have generic competition and have entered the stepped price system from May-2005 until December-2012 (Appendix I). The World Health Organization (WHO) uses the ATC code system as a classification system for drugs. The aim

is to improve drug use, with the help of the ATC system, by using it as a tool for presenting drug utilization statistics (WHOCC, 2011). For each substance it was required to go back in time and collect the time spans used from when the original received MA until the generic of the substance entered the market.

Each original pharmaceutical can have more than one generic competition in the market, therefore the dataset was narrowed down by only including the first generic that entered the market and influenced the price to decline initially. The table below shows an example of a substance called Terbinafine. There were four generics in the market for this substance but only the one from Ratiopharm GmbH was included in the dataset of this paper because it was the first generic to enter the market.

ATC-Code	Substance	Generics entered the market	Date of market entry
D01BA02	Terbinafine	Actavis Group	01-08-05
		Hexal	01-06-06
		Orifarm Generics	01-01-06
		Ratiopharm GmbH	01-05-05

Table 5.1. Selection of the generic firm for the data set

For some cases it was difficult to find the accurate dates, as they were not registered in the Athene system. In such cases, the dates were extracted from the initial application form that was sent by the particular firm to NoMA.

The data was collected chronologically from May 2005 until December 2012. Further the dataset was divided into 4 phases of the process, described below:

1. From the date the originator received market authorization until the date the original entered the market.
2. From the date the generic applied for market authorization until the date it received market authorisation.
3. From the date the generic received market authorisation until the date the generic entered the market

4. From the date the original entered the market until the date the generic entered the market.

The phases are represented in days, they were calculated by dividing the most recent date minus the previous date in the dataset i.e. phase one = the date the original entered the market minus the date the original received MA. The main interest of this paper was in phase two and three.

The descriptive statistics of the dataset collected showed the data was skewed and therefore it was not suitable to perform a T test using the mean as a comparator. Instead the Man Whitney U Test was performed as it uses the median comparator and is more suitable to compare the two periods in question, namely from 2005-08 and 2009-12. These periods were chosen because the amount of the data was satisfactory in each of them. After each phase was divided into two periods the Mann Whitney U Test was used to compare if there was any change in the time spans of each phase.

Mann-Whitney U test is nonparametric test and utilized when two independent random samples are taken from two populations. The assumptions are: the two population distributions are identical and have the same central location, called the median (Newbold, Carlson, Thorne, 2007). It is equivalent to T test, but Mann-Whitney U test is used when the assumptions of the T test are not met and when the data are ordinal. (Hilton, Brownlow, McMurray, Cozens, 2004).

The Man Whitney U test ranks the data in a scale from the lowest to the highest and compares the ranks between the two given groups. The Man Whitney U test calculates two U values in the two populations and provides us with statistics that allows us to decide when we can claim a difference between the samples. If both U values are the same it means the population samples are very mixed amongst the ranks and there is no difference between them. However if one U value is larger and the other value is smaller then it indicates a separation of the groups amongst the ranks.

ñTo test the significance of our difference we take the smaller of the two U values and examine the probability of getting this value when there is no difference between the groups. If this probability is lower than our significance level (p-value smaller than 0.05) we can reject the null hypothesis and claim a significant difference between our samplesò (Hilton et al, 2004).

In order to determine if the results were stable, another two slightly different periods were chosen from the dataset, namely 2005-09 and 2010-12. Then the Mann Whitney U test was performed again for these periods as well. The same concluding results were found between these two slightly different periods as well, which confirmed the initial results were stable.

The statistical programme PASW Statistics (formerly SPSS) version 20 was used to perform statistical analysis such as Descriptive Statistics and the Non-parametric Mann Whitney U Test. Descriptive Statistics were performed for each of the phases mentioned above and box-plots were produced to visualize the data distribution of the time span for each phase.

5.4. Qualitative data selection

In order to strengthen the findings of the 4 phases of the process, 12 interviews were conducted with relevant professionals in the field. Judgmental or purposive sampling was used to choose the participants. The decision was made thoughtfully with the help and recommendation from my contacts at NoMA, based on the judgment of who can provide the best information, so the objectives of the study can be met. The participants were people who had the required information and were willing to share it with me. This type of sampling method was appropriate for my study because the aim is to describe and develop information in areas where gaps remain and little is known (Kumar, 2001).

The goal was to reach the right informants in the field, therefore a list of many individuals who have knowledge about the topic was compiled. It was soon evident that interviewing a lot of professionals was essential, as the process of entering the market consists of many sub-processes linked together. Furthermore, I included representatives from each sub-process and

eliminated informants with similar background in order to narrow down the sample data. The sub-groups consisted of:

- Original and Generic pharmaceutical firms
- People working with the market authorization process, reimbursement and price setting of pharmaceuticals at NoMA
- Wholesalers and interest organization for pharmaceuticals in Norway.

All participants informed me about their part of the process and in addition they also included information about other sub-processes in context.

All informants were recruited by e-mail correspondence. Along with the invitation, an information letter was sent (Appendix II). The letter comprised information about the project and the importance of its conduction, as well as information about the procedure of the interview along with the participantôs rights. Initially, 14 informants were contacted and two declined. The overall response to participate in the project was positive, there were only two participants who needed more information about the project before they agreed to participate. Interviews were conducted from December 2012 to February 2013.

5.4.1. The interview

For the purpose of this thesis the semi-structured interview was used to obtain the data, as the main objective was to gain in-depth information about the process of generics entering the market. A semi-structured interview implies a mixture of structured and unstructured style of interview based on their flexibility, according to R Kumar. The unstructured interviews give the interviewer a complete freedom in structure and content, as well as formulating questions spontaneously according to the context of the discussion. The structured interviews are described as rigid in structure and contents, while the questions are set predominately and asked in the same wording and order as specified in the interview schedule (Kumar, 2001).

A covering letter with the main questions was sent to each participant as suggested by R Kumar. All the interviews were conducted face to face and with one informant at a time. A set of questions was prepared in advance, in order to steer the informant back to the topic in case they deviated away from the main topic. A recording device was used, as well as notes were taken during the interview. The covering letter is presented in appendix II.

5.5. Ethical issues

Ethical considerations are important when conducting research. An application form for a permition to conduct the interviews was sent to Norwegian Social Science Data Services (NSD). NSD did not consider the project as very personal because the questions the project addressed were not personal and did not represent a threat for the participantsô personal life or their workplace.

5.5.1. Seeking consent

Collecting information without the knowledge, expressed willingness and without the informed consent of participants is considered unethical. According to R Kumar informed consent *implies that subjects are made adequately aware of the type of information you want from them, why the information is being sought, what purpose it will be put to, how they are expected to participate in the study, and how it will directly or indirectly affect them* (Kumar, 2001).

As previously mentioned, a covering letter with information about the purpose and the importance of the project was sent along with the invitation to participate in the study. It was noted that the participation is voluntarily and that they could withdraw their consent at any time of the study. In cases where the participants were to be quoted, they were asked for their consent beforehand. In addition to the covering letter, the same information was given verbally before each interview and the informed consent was collected verbally.

5.5.2. Confidentiality

Maintaining confidentiality is another important aspect in research when accumulating data. It implies that a researcher should ensure the source of information and the identification of an individual respondent, is kept anonymous at all times (Kumar, 2001).

Confidentiality in this paper is assured to the best possible ability and the source of information is kept anonymous at all times. During the recruiting process the participant was contacted individually via e-mails in order to protect her or his anonymity. I made sure I was the only person who listened to the audio recordings of the interviews and the transcriptions were read only by me. During interviewing there was no disclosure of other participants of the same interview. My connection at NoMA is aware of most of my informants since the list of the participants was made in collaboration with her, although she does not have any information about the response. Despite this fact, it is not considered this caused any bias for the paper.

5.5.3. Avoiding bias

According to R Kumar, introducing bias into a research activity is also unethical. He defines bias as *a deliberate attempt to either hide what you have found in your study, or to highlight something disproportionally to its true existence.* Bias differs from subjectivity, as subjectivity is an integral part of the researcherôs way of thinking and is conditioned by e.g. educational background, training, competence, philosophical perspective etc. (Kumar, 2001).

The risk of introducing bias has been considered throughout the process of writing this thesis. The presentation of the results had special attention as an attempt to maintain objectivity. In some cases a recommendation of other potential participants was mentioned from the interview participants. However, it was not considered as important and was often declined in a polite way, besides the number of informants had already been covered. This thesis was requested by NoMA but there was never an attempt to influence the results of this paper in

any circumstances. Moreover, the information collected by participants was often to some extent similar. This made it easier to present the results objectively.

5.6. Validity and reliability

5.6.1. Validity

Validity in the research process intends to answer the question: Are we measuring what we aim to measure in accordance with the projectôs objectives? (Kumar, 2001). Moreover, R Kumar divides the establishment of validity into two approaches; the logical and statistical evidence approach. The statistical evidence approach implies the use of procedures that provide evidence through calculations of the coefficient of correlations between the question and the outcome variable (Kumar, 2001). The logical approach is when a link is established between each question and the objectives. Establishing the validity of tangible concepts such as age or weight is less difficult than for less tangible concepts like satisfaction, effectiveness or attitude. A wide variation of questions should be asked in order to capture several aspects of the concept, as well as demonstrate that the questions asked are measuring what they intend to measure (Kumar, 2001).

Based on the amount of interviews used to collect information about this thesis, the internal validity was established. R Kumar explains internal validity as credibility in research (Kumar, 2001). All participants included in the interview process represented every part of the pharmaceutical market. Questions used to obtain answers towards the objectives of the study provided insights, as well as the participants´ view of the process. Narrowing the amount of participants to 12 was considered appropriate since all parts of the market were covered. Certainly, the possibility to interview more representatives was there but it was time consuming and not considered as necessary.

The external validity or transferability is obtained when the research results can be generalized to other research (Kumar, 2001). Considering the external validity some of the results of this thesis might be transferable in other settings, whereas some of the results might

not due to the special pharmaceutical system used in Norway and personal opinions of the participants.

5.6.2. Reliability

A research tool is reliable if it is consistent and stable; this implies that the research tool is predictable and accurate. If a test or scale produces the same results when it is undertaken several times, under the same circumstances and with the same instrument it is said to be reliable (Kumar, 2001). In social science it is impossible to control the factors affecting reliability like:

a) The wording of questions ï the reliability can be affected if there is a use of ambiguous wording in the questions. This might result in different responses at different times.

b) The physical setting ï change in physical setting might result in different responses given by the participant.

c) The mood of the participant and the interviewer ï the mood could change from time to time and from interview to interview. This might affect the reliability of the interview.

During the process of creating this thesis a special attention was paid to the formulation of the questions used in the interview.

5.7. Limitations

While writing this thesis, there were certain limitations that I faced which the reader should consider when reading the results and conclusions of this thesis.

The first limitation met during the process of producing this thesis was the lack and of literature describing why generic firms used the time span they did before entering the market in Norway. The only literature found was the description of the pharmaceutical system in Norway. Therefore, all the reasons and arguments outlined in the qualitative results section are produced from the information extracted from the interviews conducted.

An attempt not to be influenced by the participants in the direction of their interests or cause has been highly prioritised to maintain an objective perspective. This was done by being alert during and after the interviews, so I could filter out information considered as promotions of the informantôs own causes.

Another limitation was the small sample of data available from NoMA. It is hoped that this work will stimulate further research in the field when several additional substances are available in the market, to provide en even more up-to-date picture.

Finding an explicit theoretical framework for the thesis approved to be challenging. Unfortunately, a definite theory to account for the thesis in its whole has not been formulated for the Norwegian market. Attempts to find an applicable theory have been made, however each theory considered complemented parts of the thesis. Some of the theoretical frameworks taken into account were the Price Theory for setting the price of generics, and the Market Theory describing the process of the market authorisation. Nevertheless, these theoretical frameworks did not entirely cover the main topic of the thesis.

6. Results

In this chapter the four phases will be represented with their corresponding results from both statistical analysis and interview findings.

6.1. Quantitative results

6.1.1. Descriptive statistics

Descriptive statistics of the dataset show the distribution and the time span used in each phase in the table below. The table 1 illustrates that the data is skewed and the variance within each phase is quite high. A detailed description will be given below, in the result chapter of each phase (Section 6.1.2 -6.1.4).

	N	Minimum	Maximum	Mean	Std. Deviation	Variance	Skeweness	
	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Std. Error
Phase One	53	9	605	133,94	138,589	19206,978	1,819	,327
Phase two	52	0	1080	390,56	238,133	56707,467	,885	,330
Phase tree	53	0	3414	293,83	526,249	276937,832	4,545	,330
Phase four	52	1005	10834	4039,55	1697,701	2882188,829	1,881	,327
Valid (listwise)	52							

Table 6.1. Descriptive statistics for all four phases, the variable represent number of days.

It was anticipated that there would be difference in the amount of days used within each phase. This formed the basis to employ the Mann Whitney U test for this paper. The Mann Whitney U test compares the dataset between two periods 2005-08 and 2009-12. The last phase, phase four in the table 6.1, overlaps with the first three phases as it is a sum of all phases.

Further a box-plot is shown for each phase to illustrate the data visually. Normally, the black line in the centre of a box-plot represents the median value of the dataset. Half of the data falls in the shaded box and it should be between 25% and 75% of the data spectrum. The lines

extending from the shaded box connect the highest and the lowest data points that are not considered to be outliers. These data points are referred to as whiskers. Data points larger than 1.5 times the box-length, falling outside the 25% and 75% range, are outliers and are depicted in the figures by circles. Extreme values are data points that are 3 times larger than the box-length, indicated in the figures with a star. These data points are not considered as falling inside the range of points to be displayed in the distribution. Outliers might indicate an error in the dataset (Hilton et al, 2004).

6.1.2. Phase one: From the date the originator received market authorization until the date the originator entered the market

Phase one is defined as the days used from the time point the originator received MA until they entered the market. Phase one was introduced for comparison of the time spans used in this phase with those in phase two and three.

	N	Mean	St.dev.	Min	Max	Percentiles		
						25^{th}	50(median)	75^{th}
Phase one	53	133.94	138.58	9	605	42.50	86	196

Table 6.2. Descriptive statistics for phase one

The Original firms used in average 133 days, from receiving MA until they enter the market. The median, which represents the middle observation of the dataset when arranged in increasing order, is 86,00 days. The explanation for this short usage of time might be due to the patent the originator possesses and the lacking of competitors in the market (Brekke et al, 2007).

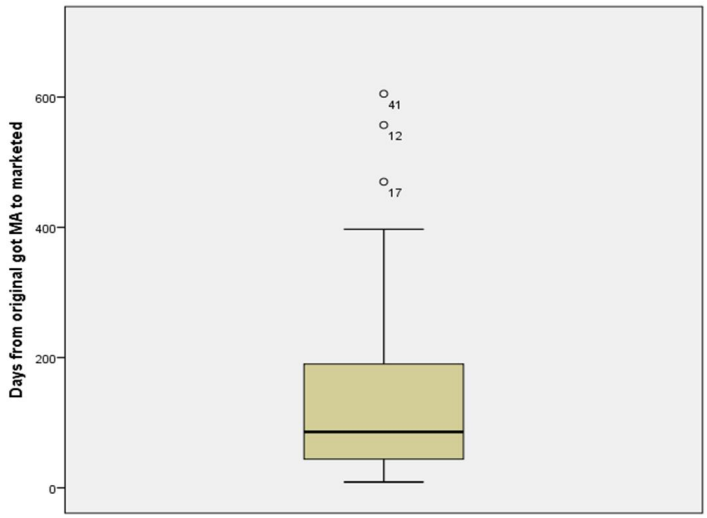

Figure 6.1. Box-plot for phase one.

Box-plot in the figure above illustrates the concentration of the data in the lower part of the box including 3 outliers. The upper whisker is wider than the lower one and the median line is in the lower part of the shaded box, implying a clearly skewed dataset. The dataset contains large outliers, which results in a greater mean than median, indicating that the data is positively skewed (Newbold et al, 2007).

The Mann Whitney U test of this phase compares the time spans between two periods 2005-08 and 2009-12. The two periods are compared in order to determine whether the original firms used longer or shorter time spans to enter the market after receiving MA.

	Entered SPS	N	Mean Rank	Sum of Ranks	Mann-Whitney U	p-value
Phase one	2005-2008	23	26.30	605	329	0.774
	2009-2012	30	27.52	826		
	Total	53				

Table 6.3. Ranks and test statistics for phase one

As expected for this phase there was not a statistically significant difference between the two periods (2005-08 and 2009-12), the p-value is 0.774, it exceeds the 0,05 p-value ceiling. In addition the mean ranks are close to each other with the values of 26,3 and 27,53. This reflects the reality of Original firms where they can enter the market without any obstacles, as

well as their interest in entering the market as soon as possible. Normally, original firms operate quickly after they receive MA.

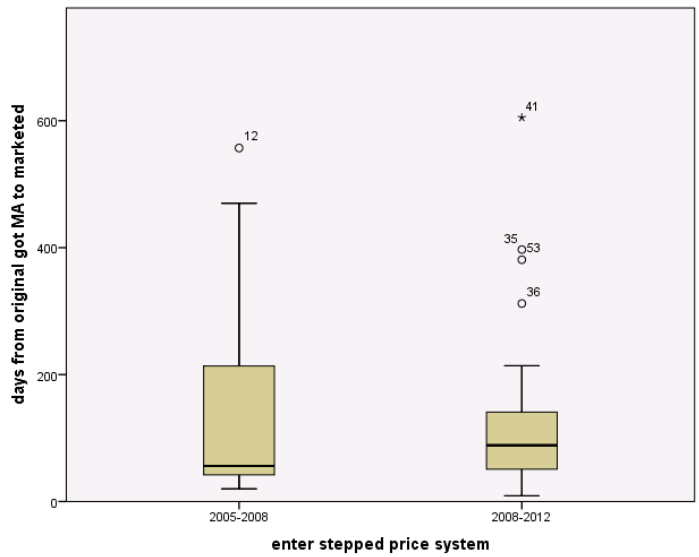

Figure 6.2: Box-plot for the two periods in phase one.

The box plot shows the median in each period is very similar even though the distribution of the data is different, suggesting that the null hypothesis is not rejected. The second period has several more outliers and the data from the 25th percentile and 75th percentile is further concentrated.

6.1.3. Phase two: From the date the generic applied for market authorization until the date it received market authorisation

The data is positively skewed in phase two as well because the mean is greater than the median. The mean is 390,56 days and the median is 357,00 days from when the generic applied for MA until they received MA as shown in table 6.4 below.

	N	Mean	St.dev.	Min	Max	Percentiles		
						25th	50(median)	75th
Phase two	52	390.56	238.13	0	1080	202.25	357	534.75

Table 6.4. Descriptive statistics for phase two

As explained in Section 2.4. Market Authorization, the process of getting MA exceeds the 210 days when we measure the total days used between applying and receiving MA.

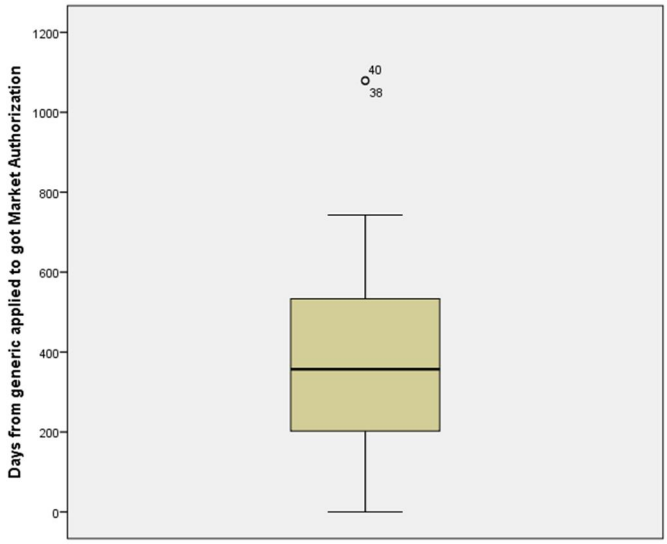

Figure 6.3. Box-plot of the phase two

The figure above shows that the majority of the data is concentrated in the middle however the data is moderately. There are two outliers presented in this dataset.

	Entered SPS	N	Mean Rank	Sum of Ranks	Mann-Whitney U	p-value
Phase two	2005-2008	23	18.41	423.50	147.50	0.001
	2009-2012	29	32.91	954.50		
	Total	52				

Table 6.5. Ranks and test statistics for phase two

The Man Whitney U test shows that there is a statistically significant difference between the two periods of 2005-08 and 2009-12 for Phase Two with a p= 0.001. In the period 2009-12 it took longer time to acquire MA approval than in the previous period of 2005-08 (Table 6.5). It took longer time to acquire MA approval during 2009-12 than it did in the previous period of 2005-08.

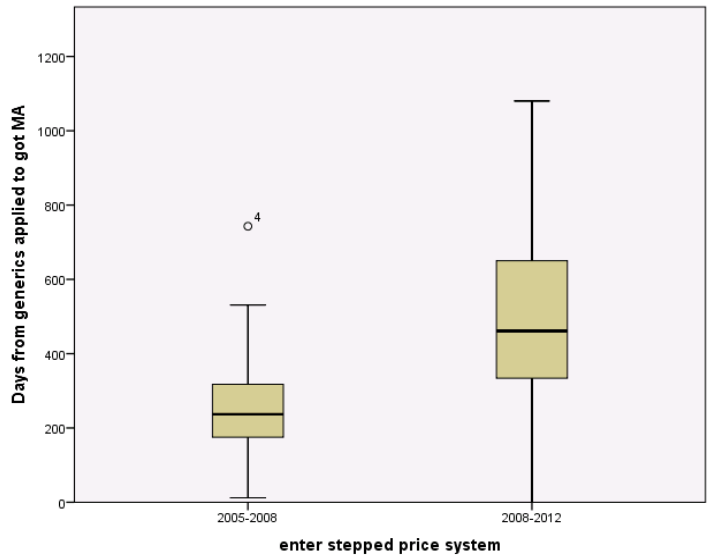

Figure 6.4. Box-plot of Phase Two for both periods

The box-plot illustrates a clear difference of the two periods in this phase. In the first period 2005-08 generics received MA much quicker than in period 2008-12. The difference of the median is wide, implying that the null hypothesis is rejected.

6.1.4. Phase three: From the date the generic received market authorisation until the date the generic entered the market

In phase three there are several steps required, from all parts of the system, before the generic can enter the market and the stepped price system. Upon deciding to enter the Norwegian market, the firm is required to apply for a selling price of the product and apply to enter the substitution list (PHIS Pharma Profile Norway, 2011; NoMAe, 2013). When this is in order the firm needs to obtain a contract with wholesalers in order to be able to sell the product. The

generic firm is often ready with a finished product while waiting for the patent of the Original drug to expire. The difficulties faced in each of these requirements are elaborated in the qualitative part below in sections 6.2.2 to 6.2.6.

The Descriptive statistics illustrate a great difference between the mean of 293,83 and median of 131. The Standard Deviation is also high. The below calculations indicate that there is a highly skewed dataset.

	N	Mean	St.dev.	Min	Max	Percentiles		
						25th	50(median)	75th
Phase three	52	293.83	526.24	0	3416	63.25	131	277.25

Table 6.8.Descriptive statistics for phase three

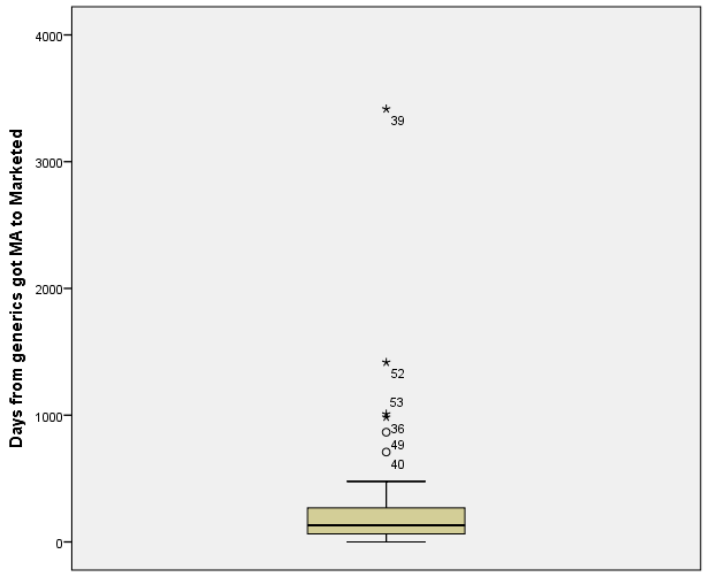

Figure 6.5. Box-plot of the data for phase three

In the figure above the box-plot of the third phase is depicted, extreme outliers as well as a broad variation between days used for each substance are observed. The minimum number of days from the time the generic received MA until they entered the market is 0 days. This is

because some of the substances do not have generic competition that already entered the market. The reason being, the firm producing the original drug choose to decrease the price and enter the stepped price system themselves. In addition, there are several outliers in this phase, for some substances it took a long time to enter the market after approved MA, i.e. for one of the substances it took 3416 days (Appendix 1). This might have occurred due to a court trial and patent violation, more details about patent violations are explained below in qualitative results in section 6.2.2.

	Entered SPS	N	Mean Rank	Sum of Ranks	Mann-Whitney U	p-value
Phase three	2005-2008	23	18.43	18.43	148.00	0.001
	2009-2012	29	32.90	32.90		
	Total	52				

Table 6.9. Ranks and test statistics for phase three

The Mann Whitney U test shows a statistical significance between the two periods with a p= 0,001. In the second period the generic firms used more time to enter the market after approved MA.

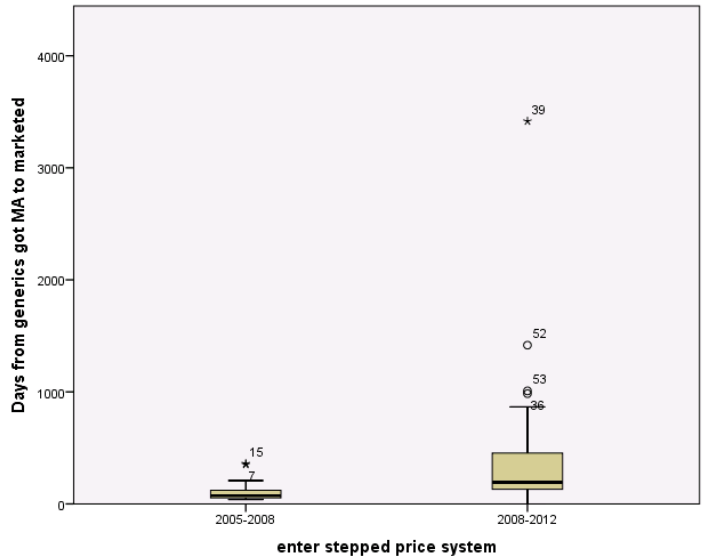

Figure 6.6. Box-plot of phase three for both periods

The box-plot illustrates the skewed distribution of the data in the two periods. The arguments to why there is a variation in the data between the two periods are commented in sections 6.2.2. to 6.2.6.

5.1.5. Phase four: From the date the original drug entered the market until the date the generic competition started

5.1.6.

Phase four is included to summarize and establish the time span of all the three previous phases in the dataset of this paper. As expected it took 4039 days on average for the 53 substances, approximately 11 years to get generic competition from the date the original entered the market. The median is 39 days smaller than the mean. Therefore the dataset is considered to be positively skewed.

	N	Mean	St.dev.	Min	Max	Percentiles		
						25th	50(median)	75th
Phase four	53	4039.55	1697.70	1005	10834	2937	4000	4641

Table 6.11. Descriptive statistics for phase four

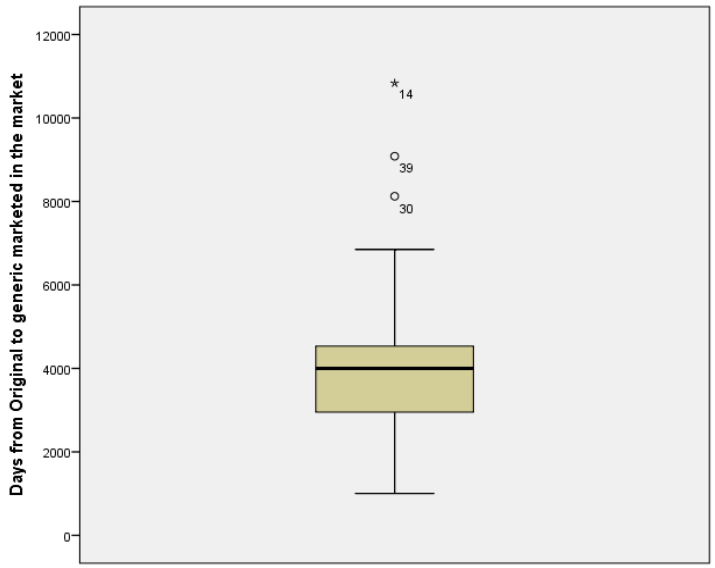

Figure 6.7. Box-plot for phase four

The box plot above shows how the data is distributed from the time point the original entered the market until when the generic entered the market. The median is in the upper part of the shaded box, implying that the data is skewed. There are 3 outliers in the box-plot; these outliers used a long time to enter the market. Some of the outcomes from phase two and three might have an impact on phase four.

	Entered SPS	N	Mean Rank	Sum of Ranks	Mann-Whitney U	p-value
Phase four	2005-2008	23	26.96	620	344	0.986
	2009-2012	30	27.03	811		
	Total	53				

Table 6.12.Ranks and test statistics for phase four

The Mann Whitney U test shows no statistical significance, with the p=0.986 between the periods 2005-08 and 2009-12 of the phase four, there is no indication in difference in the time span used between substances. The hypothesis that there might be a difference in the time spans between the two periods is not true. So the null hypothesis is not rejected.

6.2. Qualitative results

In this part of the thesis an attempt was made to find out why it took so long time for some generics to enter the market. Why did generic products use longer time to enter the market in the second period? When does a generic firm start the process of entering the market?

6.2.1. The obstacles during the MA process

One of the inquires of this paper was to examine the reason for using a clock-stop during the MA process. The answers received from informants suggested the clock-stop is there to cover unanticipated events in the MA process due to variations from one product to another. In some cases the EMA cannot come to an agreement internally between member states and requires more information about the pharmaceutical, chemical or bio-similarity. Other reasons can be requirements to improve the wording and the appropriate translation of the information in the Norwegian language. In some cases the firm does not send the translated version to NoMA, regardless of this NoMA might release the MA, however, the firm is not allowed to

start selling before the translation is in place. Potentially, the name of the drug may be inappropriate, so the firm is required to find another one. This process of arguments back and forth can sometimes turn into a long discussion. The generic firms reported that sometimes it was time consuming to gather the required documentation for MA.

The informants from both the original and generic firms, as well as from NoMA reported that when applying for MA the Centralised Procedure was mostly used. It is more convenient for the firms to go through the Centralised Procedure because when MA is granted it can be utilized in all member states.

All the informants from NoMA and from the firms reported there was a queue in processing the MA application because of the lack of the capacity at NoMA. The 210-day application process exceeded and it was reported that the queue went up to 3 years for a MA process to complete. Therefore in 2008 NoMA changed this by employing more workers, which resulted in increased resource capacity for processing the application. Another 3 years were spent in order to eliminate the queue that had built up previously. Many of the substances in the dataset of this paper entered the market during the queue period. This situation could have potentially delayed the MA application process even further. After the queue at NoMA was eliminated, all the interviewed firms expressed their satisfaction with the processing of MA at NoMA.

One participant from a firm stated:

é *but now there is no queue when applying MA and we are very satisfied with that.*

6.2.2. The Patent obstacles

Generic firms have to wait for the patent of the originator to expire in order to enter the market. In the interviews conducted it was reported by all the informants that until recently in Norway, Pharmaceutical firms actually received a process patent when innovating a new product as opposed to a product patent. The Process patent protects the process of how the

drugs are produced and prepared, but it does not protect the product itself. There were cases where generic companies found new ways of producing the drug and entered the market before the patent of the Original drug expired. This situation gave rise to conflicts of interest and sometimes ended in a court trial. These court trials have extended the average time to complete the phase of entering the marked after getting MA.

However, currently only the product patent is used on innovative products and soon there will be no original product with a process patent remaining in the market. The informants confirmed that it was easier to deal with product patents compared to the process patents. For example, a generic company would not be tempted to find another process of producing the drugs while at the same time an original company would not have to worry about losing itôs exclusivity in the market.

Original pharmaceutical companies are interested to extend the patent duration and can sometimes complicate the patent time by possessing several patent types for the same drug; such as for substance, different dosage forms and other parts of the drug. To avoid patent violation the generic companies are obliged to try to find out about all the different patent types an Original drug might have, before they enter the market. There were cases where the patent was violated by a generic company and a court trial followed as the generic had missed a patent date. The generic companies claimed they were interested to avoid court trials and are careful when entering the market.

Generic firms apply for MA long before the patent of Original expires so they can be ready to enter the market when the patent expires. This has an effect on the time it takes to complete the phase three - from approved MA until they enter the market.

6.2.3. Norway is a small market

While analysing the data it was observed that many generics had MA but they never entered the market. A possible explanation for this may be the firm possessed the MA in all member states but chose to sell in only some of the states. It should be noted that in some cases

generic companies might not enter the Norwegian market straight away after they receive MA, there could be business or other reasons for not doing so and therefore this introduces another delay to the process. One representative from the firms said:

ñ*Before we decide producing a generic we check to what extent the original is sold, if it is an important drug with high profit we decide to compete with other generic firms in entering the Norwegian market****ò***

Another representative from the firms said:

ñ*Norway is a small country compared to Germany and UK, therefore not a priority for us to enter the market right away****ò***

6.2.4. Production issues of Generic Drugs

Generic firms claimed that when attempting to produce a drug, firstly they have to establish the pharmaceutical development of the drug and also determine which production company should supply the chemicals required for the substance wished to be produce. In some cases, after starting the process of developing the drug, the original firm bought the chemical supply company that would provide the generic firm with the chemicals. One representative informed:

ñ*After we found a supplier for the chemicals we needed for the production and came to an agreement, an original producer bought the whole factory.****ò***

This resulted in the delaying of the developing process for generic firms, as the generic firms have to find other supply companies that met their requirements before an actual business agreement.

6.2.5. The substitution list and reimbursement schemes

The generic drugs need to enter the Substitution List Scheme in order to be reimbursed by the Norwegian Health Insurance Scheme. Informants at NoMA claimed, when the first generic

product receives a price from NoMA, the Stepped Price System department starts to consider whether the drug can be a part of the Substitution List Scheme.

The entrance in the Substitution List Scheme is not problematic in most cases. The effect of the drug has already been validated during the process of receiving MA. In addition to double checking the bio-similarity of the drug, the Substitution List Group considers whether the generic product is substitutable with the original product. The questions addressed to this process are: Is it possible to take the generic product in addition to the original, if the patient might misunderstand, and what are the consequences of double dosage? Can the patient choose not to take the drug at all because they are afraid of the effects of the new drug? All these consequences are considered in both short and long term effects before the Substitution List Group agrees to reimburse the drug. The generic drug will enter the substitution list immediately if there are no other factors to be considered. If there is insecurity about the use of the drug in different patient groups, a wider discussion begins with all the parties involved including patients, doctors, specialists and patient organisations. In some cases before the decision is made, open hearing sessions are organized to get the opinion of all the parties involved. As a consequence the processing time for a generic product to enter the substitution list might exceed the 180 days limit by an additional 6 weeks or even up to 1 year more.

6.2.6. Wholesalers and the Norwegian market

All informants mentioned that they believe the wholesalers have a great power in the Norwegian pharmaceutical market. For a drug to enter the market an agreement contract between the pharmaceutical firm and the wholesaler needs to be completed. The wholesalers negotiate the purchase price with these firms. When a generic drug is ready to sell it enters the Stepped Price System. Original firms can also enter the Stepped Price System if they choose to compete with generic firms during the wholesalerôs negotiations on finding the most suitable drug. Both original and generic firms commented that the wholesalers have various strategies when selecting which product to buy. They might focus on a low price, which they can get from a generic firm, or they might focus on professional and quality profile, in which case they will prefer the original firm.

The generic producers interviewed explained sometimes when they possessed MA and were ready to launch, the wholesalers made an agreement with original producer even with a higher purchasing price and the stepped price was launched with original, but the generic never entered the market or was delayed for a long period of time. The generic production firms claimed that at this time of the process a lot of money had been invested and lost as a consequence of how the stepped price functioned. In the dataset presented this phenomenon was observed, but only twice. It seems that for now this appears rarely, however, it might reappear in the future. This is the reason why in the phase two and three, the time span starts from day 0, because there is no generic drug in the market and only the original entered the stepped price system after its patent expired.

5.2. Other findings

The Stepped Price System cannot be established if the original drug does not have a competition i.e. a generic that is ready to enter the market.

Both wholesalers and generic companies did complain about the pharmaceutical act where they are obliged to offer the drug at a stepped price, even if there are production problems with the drug and the pharmacy might not have the drug in stock. The wholesalers might only have the original drug in stock in which case they are obliged to offer the original drug at the stepped price, while incurring the cost themselves. This would be the case if NoMA notifies the entrance of stepped price before the wholesalers made an agreement with any production firm to sell the drug at stepped price.

Pharmacies are obliged to sell the cheapest product in order for the government to reimburse them. They are obliged to deliver the medicine required by the patient at all times. As a consequence the wholesalers often make an extra agreement with the generic firm called Compensation Claim Agreement. They agree that if the generic firm cannot deliver the generic product to the wholesalers then they have to pay the full price of the original product. This means the generic firms will end up paying a much larger amount of money per medicine to the wholesaler if they donąt deliver, while protecting the patient from such costs. One participant said:

ñ*This is one of the reasons that withdrew the producers away from the Norwegian market.***ò**

The selling agreement between the wholesaler and the production firm of the drug in the Stepped Price System often lasts one year. Therefore it is important for generic firms to be the first to enter the market after the original, so they can get well known among the patients and get the chance to sell their product. The pharmacies are obliged by law to offer the drug on stepped price either as a generic or original, once the stepped price is established.

There are a lot of generics per substance with MA that never enter the Norwegian market. The informants gave several reasons for this, one of them was that the Norwegian market is small

and the second reason is the substance representing a small group of users and does not sell profitably. The generic firms are not interested because it is not profitable to enter the market. The third reason might be the way Norwegian market is regulated; it does not provide room to have several generics in the market at a time.

6.4. Summary of results

In this paper it was discovered that in order for a generic medicine to obtain MA it takes on average 357 days (median), while a generic used 131 days according to median to enter the market after approved MA. During the interviews several reasons were identified for this time span used, listed below:

- Various obstacles that affect the MA process.
- Patent obstacles and complications that affect the overall time span.
- Norway is a relatively small market and therefore less attractive for some generic companies.
- Production issues and challenges faced by generic firms
- In some cases, the substitution list and reimbursement scheme processes can cause delays to the overall time span.
- Once the original drug patent expires, the original firms can choose to enter the stepped price system and create competition for generic firm, which causes a delay in entering the market.

7.Conclusion

Generic drugs are an important element in health economy as they contribute to the decline of pharmaceutical prices. There are several processes required to complete before a generic drug can enter the market. For each of these processes, which are called phases in this paper, there are regulations that apply. These regulations need to be followed in order for a firm to enter the market. Before a generic drug enters the market the firm has to develop the drug, apply for MA, enter the substitution list in order to be financed by the NIS, and finally wait for the patent of the original drug to expire before it can enter the market.

The sample data gathered from NoMA included 53 substances and each substance had an original as well as a generic drug present in the Norwegian market. The data analysis revealed that generally an original drug would be free of generic competition for 11 years on average Furthermore, once a generic firm applies for MA it takes 357 days (median) on average to get approval. Once approved MA, generic firms used 131 days (median) on average to enter the market.

In addition to being a small market for pharmaceuticals compared to other European countries, generic companies experience a high competition to enter the Norwegian market, because of the vertical integrated market. It was claimed that these two reasons withdrew the generic firms from the Norwegian market.

The findings of this paper might have an impact in the future of socio-economic analysis with regard to the real-price adjustment for pharmaceuticals. As highlighted earlier, the time span might be a contribution in evaluation of cost-effectiveness analysis in health care. The results obtained can provide public health decision-makers with useful information regarding the resource allocation. Potentially, these findings might be used by NoMA for the purpose of pharmaceutical reimbursement to compare the time-span results from this thesis with those presented by the pharmaceutical firm, in their pharmacoeconomic analysis. Particularly, when a comparative drug applies for reimbursement for the next 5 years. Subsequently, these results might help NoMA to estimate a more accurate price path prediction of the drug.

Regarding future studies, it would be desirable to conduct a follow-up study of time span including more data when these are available, in order to examine whether the trend of time span has altered or remained stable. Furthermore, a case study to investigate some substances in detail would be of great interest. Information about why some particular substances used less time to enter the market can be insightful and might alter the policy within the public health decision-makers and the pharmaceutical companies. This in combination with the findings presented here would probably lead to new effective solutions.

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Appendix I

Table 1: information about the substances and the days calculated in four phases included in the paper.

ATC code	Substance	entered stepped price system	Days from Original got MA to marketed	Days from Generic applied to got MA	Days from Generic got MA to Marketed	Days from original to generic marketed
N06AB06	Sertraline	01-nov-05	56,00	179,00	74,00	3137,00
A02BC03	Lanzoprazole	01-mai-05	32,00	192,00	44,00	4079,00
D01BA02	Terbinafine	01-mai-05	44,00	168,00	60,00	4048,00
M01AC06	Meloxicam	01-sep-05	252,00	743,00	51,00	2984,00
M05BA04	Alendronat	01-des-05	208,00	202,00	43,00	3167,00
G04CA02	Tamsulosin	01-feb-06	47,00	195,00	72,00	2922,00
N02CC01	Sumatripan	01-juni-06	29,00	203,00	351,00	4474,00
A10BB12	Glimepiride	01-des-05	264,00	239,00	63,00	2983,00
N05AX08	Risperidone	01-des-06	40,00	242,00	208,00	4110,00
G04CB01	Finasteride	01-mai-07	21,00	160,00	78,00	5068,00
C02AC05	Moxonidine	01-mai-07	202,00	237,00	76,00	2844,00
N05AH04	Quetiapine	01-juni-07	557,00	531,00	45,00	1005,00
N06AX16	Venlafaxine	01-juni-07	219,00	390,00	56,00	2783,00
C07AB02	Metorpolol	01-okt-07	21,00	12,00	39,00	10834,00
R01AD08	Fluticasone	01-apr-07	53,00	158,00	360,00	4976,00
G02CB03	Kagergolin	01-juli-07	278,00	241,00	122,00	4929,00
N04BC06	Kabergolin	01-juli-07	470,00	241,00	122,00	2952,00

ATC code	Substance	entered stepped price system	Days from Original got MA to marketed	Days from Generic applied to got MA	Days from Generic got MA to Marketed	Days from original to generic marketed
N02AB03	Fenatyl	15-juli-05	81,00	158,00	165,00	3636,00
A04AA01	Ondansetron	01-sep-05	20,00	245,00	104,00	5479,00
A02BC02	Pantoprazol	01-des-07	111,00	392,00	161,00	4383,00
N05AH03	Olanzapin	01-jan-08	88,00	449,00	42,00	2832,00
L02BB03	Bicalutamid	01-aug-07	51,00	171,00	96,00	3864,00
C10AA05	Atrovasatatin	15-nov-08	48,00	520,00	58,00	4049,00
N06DA02	Donepezil	01-apr-09	104,00	379,00	85,00	3745,00
A08AA10	Sibutramin	01-apr-09	30,00	650,00	157,00	2265,00
N04BC04	Ropinirol	01-juni-09	160,00	454,00	429,00	3575,00
C09CA01	Losartan	15-sep-09	24,00	335,00	64,00	4336,00
C09DA01	Losartan og diuretisk	15-sep-09	51,00	671,00	251,00	4293,00
J01CA08	Pivmecillinam	01-mai-09	60,00	461,00	130,00	8125,00
N06DA03	Rivastigmin	01-des-09	106,00	268,00	198,00	3684,00
C07AB07	Bisoprolol	01-mars-10	68,00	507,00	148,00	2635,00
N06AB10	Escitalopram	01-mars-10	62,00	676,00	35,00	2724,00
S01EE01	Latanoprost	01-apr-10	115,00	637,00	227,00	4534,00
J05AB11	Valaciklovir	01-jan-10	397,00	334,00	132,00	4762,00
L04AA06	Mykofenolatm	01-juli-10	312,00	192,00	984,00	2996,00
C08CA13	Lerkanidipin	01-aug-10	119,00	459,00	454,00	3621,00
L02BG03	Anastrozol	15-mai-10	41,00	1078,00	412,00	4853,00
N02AA01	Morfinsulfat	15-jan-11	12,00	227,00	3416,00	9084,00
D05AX02	Kalsipotriol	01-apr-11	28,00	1080,00	709,00	6849,00
B01AC04	Klopidogrel	01-des-09	605,00	651,00	286,00	2066,00
C09CA03	Valsartan	01-apr-10	214,00	230,00	193,00	2393,00

ATC code	Substance	entered stepped price system	Days from Original got MA to marketed	Days from Generic applied to got MA	Days from Generic got MA to Marketed	Days from original to generic marketed
L01AX03	Temozolomid	01-juni-10	9,00	63,00	47,00	2207,00
L02BG04	Letrozol	01-aug-11	141,00	416,00	193,00	4748,00
L02BG06	Eksemestan	15-juli-11	91,00			4000,00
N07BC01	Buprenorfin	23-des-10	75,00	498,00	93,00	4047,00
C09DA03	Valsartan og	01-des-11	56,00	406,00	477,00	4293,00
R06AX27	Desloratadin	01-mars-12	17,00	0,00	0,00	4046,00
S01ED51	Latanoprost/Timorol	15-apr-12	86,00	595,00	866,00	3805,00
C09CA06	Kandesartan	01-mai-12	129,00	567,00	102,00	4961,00
C09DA06	Kandesartan og Diuretica	01-mai-12	138,00	536,00	133,00	4138,00
R03DC03	Montelukast	01-sep-12	86,00	658,00	1417,00	5053,00
C09CA04	Irbesartan	01-sep-12	381,00	717,00	1009,00	2692,00

Appendix II

Interview question guide

The interview will not follow a tight program, but it will rather be like a conversation. The conversation shall start with questions about the experience with generic drugs related to the processes to enter the market. If the conversation deviates the questions below were used.

1. When does generic firms apply for Market Authorisation (MT)
2. What do you think about the time span used to approve MT?
3. There are many generic products with MT but they have not entered the market yet, what may be the reason? What can be done to get these products to enter the market faster?
4. Is it likely for original drugs with low turnover not to get generic competition because it will not be profitable?
5. Do you make a conscious decision choice of applications with high profit above applications with low profit, when there are many applications? (Directed to NOMA)
6. Can price regulation in Norwegian marked cause unwillingness to sell generic products in Norway?
7. What are the reasons for waiting up to a year to enter the market after getting MA?
8. What do you think about the stepped price system?
9. What would an ideal market for generics look like?

Invitation to participate in an interview in relation to a Master Thesis

I am a student at the Master´s programme Health Economics, Policy and Management at the University of Oslo, and I am at the moment working on my Master Thesis.

The theme for the thesis is ñGeneric Competition in Pharmaceutical Industry, - how fast does generics get into the step price system?ò The focus will be in studying the process and the time span between the dates of application for market authorization (MA) and the dates the step price is established. The aim of the study is to assess whether these processes and time spans are comparable between different drugs and can be formalized and used to predict price path (prisbaner) in analyses of health economy or cost effectiveness. The Norwegian Medicines Agency (NoMA) is responsible for setting maximum pharmacy purchase prices and maximum reimbursement price for affected medicines (both generic and original). A special price model is used for generics. Step price model (Trinprismodellen) is a scheme that ensures price fall in pharmaceuticals stepwise, by predefined rates. The model was introduced in January 2005 to reduce the costs of National Insurance Scheme. Pharmaceutical prices are important variables for cost effectiveness analysis. Many of these analyses have a time span of several years. Therefore prediction of pharmaceutical prices is a very important factor. The biggest change in future prices are as usually when generic competition is established.

In order to complete my study I wish to interview those representatives at NoMA that work with market authorisation, step price and list of substitutable drugs (bytteliste). In addition I would like to interview representatives from the pharmaceutical industry that offer step price products, both suppliers of originators and generics.

The method for collecting the needed information is collecting data from NoMA´s database and interviews where the informant will be able to tell his/her experiences with and opinion of the process. The interview will not follow a tight plan. I will use a tape recorder in addition to taking notes. This is to enhance the quality of the quotes, and the recording will be deleted after the project has been finished. The interview will take about one hour, and the informant can decide the time and place. The quotes that will be used, or specific opinions or perceptions that are emphasized greatly, will be checked with the informant before the thesis is handed in for evaluation. No names of informants will be used in the thesis.

Participation in the study is of course voluntary and the consent of the participation can be withdrawn as long as the study is in progress without any cause being needed. As a researcher I am a subject of confidentiality and must therefore treat all data confidentially.

Feel free to contact me, or my supervisor if any question.

Regards

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Appendix III

Statistical outputs from PASW Statistics (formerly SPSS) version 20

Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation	Variance	Skewness	
	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Statistic	Std. Error
Phase_one	53	9	605	133,94	138,589	19206,978	1,819	,327
Phase_two	52	0	1080	390,56	238,133	56707,467	,885	,330
Phase_tree	52	0	3416	293,83	526,249	276937,832	4,545	,330
Phase_four	53	1005	10834	4039,55	1697,701	2882188,829	1,881	,327
Valid N (listwise)	52							

Statistical outputs for phase one

Descriptive Statistics

	N	Mean	Std. Deviation	Minimum	Maximum	Percentiles		
						25th	50th (Median)	75th
days_from_MA_to_marketed	53	133.94	138.589	9	605	42.50	86.00	196.00
enter_sps	53	1.57	.500	1	2	1.00	2.00	2.00

Ranks

	enter_sps	N	Mean Rank	Sum of Ranks
days_from_MA_to_marketed	1	23	26.30	605.00
	2	30	27.53	826.00
	Total	53		

Test Statistics[a]

	days_from_MA_to_marketed
Mann-Whitney U	329.000
Wilcoxon W	605.000
Z	-.287
Asymp. Sig. (2-tailed)	.774
Exact Sig. (2-tailed)	.779
Exact Sig. (1-tailed)	.390
Point Probability	.003

a. Grouping Variable: enter_sps

Statistical outputs for phase two

Descriptive Statistics

	N	Mean	Std. Deviation	Minimum	Maximum	Percentiles		
						25th	50th (Median)	75th
Days_from_applied_to_got_MA	52	390.56	238.133	0	1080	202.25	357.00	534.75
enter_sps	53	1.57	.500	1	2	1.00	2.00	2.00

Ranks

	enter_sps	N	Mean Rank	Sum of Ranks
Days_from_applied_to_got_MA	1	23	18.41	423.50
	2	29	32.91	954.50
	Total	52		

Test Statistics[a]

	Days_from_applied_to_got_MA
Mann-Whitney U	147.500
Wilcoxon W	423.500
Z	-3.427
Asymp. Sig. (2-tailed)	.001
Exact Sig. (2-tailed)	.000
Exact Sig. (1-tailed)	.000
Point Probability	.000

a. Grouping Variable: enter_sps

Statistical outputs for phase three

Descriptive Statistics

	N	Mean	Std. Deviation	Minimum	Maximum	Percentiles		
						25th	50th (Median)	75th
Days_from_got_MA_to_Marketed	52	293.83	526.249	0	3416	63.25	131.00	277.25
enter_sps	53	1.57	.500	1	2	1.00	2.00	2.00

Ranks

	enter_sps	N	Mean Rank	Sum of Ranks
Days_from_got_MA_to_Marketed	1	23	18.43	424.00
	2	29	32.90	954.00
	Total	52		

Test Statistics[a]

	Days_from_got_MA_to_Marketed
Mann-Whitney U	148.000
Wilcoxon W	424.000
Z	-3.418
Asymp. Sig. (2-tailed)	.001
Exact Sig. (2-tailed)	.000
Exact Sig. (1-tailed)	.000
Point Probability	.000

a. Grouping Variable: enter_sps

Statistical outputs for phase four

Descriptive Statistics

	N	Mean	Std. Deviation	Minimum	Maximum	Percentiles		
						25th	50th (Median)	75th
Original_to_generic_marketed	53	4039.55	1697.701	1005	10834	2937.00	4000.00	4641.00
enter_sps	53	1.57	.500	1	2	1.00	2.00	2.00

Ranks

	enter_sps	N	Mean Rank	Sum of Ranks
Original_to_generic_marketed	1	23	26.96	620.00
	2	30	27.03	811.00
	Total	53		

Test Statistics[a]

	Original_to_generic_marketed
Mann-Whitney U	344.000
Wilcoxon W	620.000
Z	-.018
Asymp. Sig. (2-tailed)	.986
Exact Sig. (2-tailed)	.989
Exact Sig. (1-tailed)	.495
Point Probability	.004

a. Grouping Variable: enter_sps